Listeria monocytogenes: Low Levels Equal Low Risk

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ABSTRACT

Because of the public health significance of L. monocytogenes, U.S. regulatory agencies established a policy whereby ready-to-eat foods contaminated with the organism at a detectable level are deemed adulterated. This “zero tolerance” policy, however, makes no distinction between foods contaminated at high and low levels. We have reported elsewhere that a survey of over 31,000 ready-to-eat retail food samples, representing eight product categories, showed an overall prevalence rate of 1.82% for these foods. In this study, we used the food survey data in combination with concurrent data regarding illness in the population consuming the foods, together with other variable factors, to derive a dose-response model. The confidence interval for prevalence was 1.68 to 1.97%. L. monocytogenes levels, which ranged from −2 to 6 log CFU/g, were adequately described by the distribution beta (0.29, 2.68, −1.69, 6.1). An exponential dose-response model was obtained, with an R value (essentially the probability of a single cell causing illness) of 1.76 × 10−2 for the population at the highest risk. A microbial risk assessment based on the model shows that an alternative to the zero tolerance strategy has a greater risk reduction potential and suggests that a management strategy focusing on the concentration of L. monocytogenes rather than its presence alone may have a greater impact on the improvement of public health by facilitating the development of control measures to limit the maximum levels of L. monocytogenes in foods.

Listeriosis, an infection caused by Listeria monocytogenes, occurs relatively infrequently. The Centers for Disease Control and Prevention (CDC) have estimated that 2,500 cases occur each year (5 cases per million people), compared with, for example, 1,400,000 cases of salmonellosis (28). More recently, on the basis of data from the FoodNet active surveillance program, the CDC reported a listeriosis frequency of 3 cases per million people for 2000 and 2001 (7–9). However, although the incidence of listeriosis cases is comparatively low, the listeriosis case fatality rate of 20% is one of the highest for a foodborne illness (28); thus, it is clearly important to develop appropriate risk management strategies for L. monocytogenes.

Almost all listeriosis is foodborne (28). One of the factors that makes L. monocytogenes particularly difficult to control in foods is that, unlike most foodborne pathogens, it can grow at refrigeration temperatures. L. monocytogenes is considered ubiquitous in the environment and has been isolated from a wide variety of foods, including dairy products, meat and poultry products, vegetables, seafood, and other products (32, 39). This organism has been isolated from food-processing environments (2, 14, 17), from retail products (16, 33), and from consumers’ homes (3, 11). L. monocytogenes has also been isolated from the intestinal tracts of normall, healthy humans (34). Although listeriosis can occur in apparently healthy individuals, it is primarily pregnant women and their neonates, elderly people, and immunocompromised individuals who are considered to be at the highest risk (34). Because of the public health significance of L. monocytogenes, U.S. regulatory agencies established a policy whereby ready-to-eat (RTE) foods contaminated with the organism at a detectable level are deemed adulterated. Since the establishment of this “zero tolerance” policy in the 1980s, the food industry has made major changes in an effort to eradicate the organism from RTE products and processing environments (35, 36). The prevalence of L. monocytogenes in certain products has been reduced (26). However, data suggest that L. monocytogenes cannot be eliminated from the environment or from all food products, and it continues to contaminate RTE products periodically despite the implementation of extensive control measures (35). The negative impact of a zero tolerance policy on efforts to control L. monocytogenes has recently been described (35).

One of the goals of the Healthy People 2010 initiative (38) is to reduce illnesses caused by L. monocytogenes by 50%. The regulatory approach currently being taken to meet this goal concentrates on further reducing the prevalence of L. monocytogenes in RTE foods and continues the zero tolerance standard for all RTE foods. Here, we report findings from a microbial risk assessment that suggest that an alternative to this management strategy may have a greater impact on the improvement of public health by facilitating the development of more effective control measures to achieve the objective.

MATERIALS AND METHODS

Determination of probabilities of illness for different dose levels. A major difficulty in undertaking a microbial risk assessment for L. monocytogenes has been the determination of the in-
fectious dose required to cause illness in humans. An infectious dose is typically determined by feeding studies, i.e., feeding known quantities of a microorganism to a subject to determine the level required to cause illness (20). Owing to the high case fatality rate for listeriosis, human feeding trials carry an unacceptably high risk. Therefore, direct measurement of the infectious dose of L. monocytogenes for humans has not been undertaken. As a result, some dose-response assessments have relied on animal data (6, 20). The combination of contamination levels determined in food surveys and data on illnesses determined in epidemiological investigations provides an alternative derivation of a dose-response relationship based on data that are more directly relevant to humans.

In theory, it is conceivable that any dose level can cause illness in the susceptible population. Assuming that a single ingested L. monocytogenes cell is capable of causing infection and that when N organisms are consumed each of them has the same probability of causing illness results in an exponential dose-response model (5, 6, 18, 19):

$$P(I) = 1 - e^{-RN}$$ (1)

where P(I) is the probability of listeriosis at dose N, and R is the model parameter specific to the pathogen of concern. According to equation 1, the probability of acquiring listeriosis increases exponentially as the number of cells consumed increases. When a single organism’s probability of causing infection is small, this probability is approximately equal to the value of the model parameter, R. As described below, the model parameter is estimated so as to provide a purposely conservative model (5, 6), thereby resulting in an overall conservative assessment of risk in our study.

The model parameter was derived on the basis of the levels of L. monocytogenes contamination in foods, the number of listeriosis cases in the population consuming the foods, the size of the population (only individuals at higher risk were considered), the number of servings consumed, and the serving size. The parameter R was determined according to the approach described by Buchanan et al. (6). The prevalence of L. monocytogenes in the foods consumed and the shape of the concentration distribution defined the fractions of servings that were contaminated at various levels. In deriving the R value with the use of a spreadsheet in Excel (Microsoft Corp., Redmond, Wash.), calculations were repeated until the actual number of listeriosis cases was predicted on the basis of all other input variables, including prevalence and concentration distribution.

Data used in the assessment. Since almost all listeriosis is foodborne (28), we made the conservative assumption that RTE foods are a primary source of consumer exposure to L. monocytogenes. The levels of L. monocytogenes contamination in foods were obtained from a food survey reported elsewhere (16). Food samples collected in that survey represented eight RTE product categories: luncheon meats, deli salads, fresh soft cheeses, bagged leafy vegetable salads, blue-veined cheeses, soft mold-ripened cheeses, smoked seafood, and seafood salads. The data from the food survey were used to quantify the prevalence and concentration distribution of L. monocytogenes in the foods consumed.

The number of listeriosis cases was obtained from the CDC (1). In order to relate listeriosis to L. monocytogenes exposure, we used illness data from the Maryland and northern California FoodNet sites at which the food survey was conducted (16). The food survey was carried out over 2 years (2000 and 2001) when the CDC were conducting a listeriosis case-control study at the FoodNet sites. There were 53 listeriosis cases reported for the FoodNet sites in 2000 and 2001, which would result in an estimated 106 cases for the 2-year sampling period given a twofold multiplier for underreporting (28).

According to Census 2000 (37), the size of the population of the United States was 288,800,000, and the sizes of the populations for the Maryland and California sampling sites where the food survey was conducted were 4,620,000 and 2,220,000, respectively. Therefore, 2.37% of the U.S. population resided in the sampling regions. The size of the higher-risk population was estimated to be 25% of the U.S. population (15, 29), a percentage that also applied to the populations in the regions in which the food survey was conducted and in which illness data were obtained.

The number of servings consumed by the higher-risk U.S. population was estimated to be $1.11 \times 10^{10}$ per annum for the eight product categories included in the food survey on the basis of national consumption data used in the U.S. Food and Drug Administration-Food Safety and Inspection Service draft L. monocytogenes risk assessment (39). These data were adjusted to reflect the actual population in 2000. The number of servings consumed by the higher-risk population in the sampling regions over the 2-year sampling period was calculated as $(1.11 \times 10^{10}) \times 2.37\% \times 2 = 5.26 \times 10^8$. Serving size was given a value of 50 g on the basis of the weighted median serving size calculated from the fraction of servings and the median serving size for each of the eight RTE product categories (data not shown).

Assumptions. The theoretical assumption underlying the exponential model is that a single L. monocytogenes cell is capable of causing infection (i.e., listeriosis) in a consumer upon ingestion given that the cell is pathogenic and the host is susceptible (6, 40). This assumption also underlies another nonthreshold model established to describe the dose-response relationship for L. monocytogenes (13). The exponential model is also based on the assumptions that each member of the susceptible population responds the same and that the effect of each organism is independent of that of others. Although the exponential model is an expression of the binomial probability of illness, the model is inherently limited in that no experimental data involving L. monocytogenes in humans were used in its selection. Unlike non-life-threatening foodborne pathogens, L. monocytogenes has not been subjected to human volunteer feeding studies because of its high hospitalization and case fatality rates (6, 28). While the exponential model is one of the well-recognized models, when the mathematical relationship (equation 1) is extrapolated to describe the probability that illness will be caused by low dose levels, consistency between theory and reality has not been experimentally proven.

For this study, we further assumed that all L. monocytogenes organisms in foods are pathogenic, consistent with current regulatory policy. We made the conservative assumption that all listeriosis cases at the Maryland and California FoodNet sites resulted from the consumption of the eight product categories by the higher-risk population. Some factors that may influence risk that were not explicitly modeled in our risk assessment include variability in virulence among L. monocytogenes subtypes (41) and food matrix effect.

Determination of prevalence uncertainty and concentration distribution. The L. monocytogenes prevalence used in the risk assessment was the overall observed prevalence and the 2.5th and 97.5th percentiles of the prevalence uncertainty distributions. Data used for calculating prevalence uncertainty levels were the total number of samples (n) and the number of positive samples (s) obtained in the food survey (16). The uncertainty distributions
were defined as beta \((s + 1), (n - s)\) for the upper bound and beta \((s, (n - s + 1)\) for the lower bound \((4, 40)\). The distribution functions were input into Analytica (version 2.0, Lumina Decision Systems, Los Gatos, Calif.), and simulations were run (30,000 iterations) according to previously reported methods \((12, 30)\). The 2.5th- and 97.5th-percentile values were determined on the basis of the results of the simulations.

The concentration distribution for \(L.\) monocytogenes was determined on the basis of the food survey data. Samples found to contain \(L.\) monocytogenes in the food survey were grouped into various concentration ranges with 1-log intervals. In the survey study \((16)\), the lowest concentration in a positive sample was represented by the most probable number (MPN) pattern \([1/1, 0/3, 0/3, 0/3]\) for cultures of 25-, 1-, 0.1-, and 0.01-g portions of the sample. The amount of a sample taken for both screening and enumeration was used in the estimation of the lowest concentration for a positive sample. This concentration was highly likely to be \(\leq 0.09\) organisms per g, i.e., \(0.09\) MPN/g \((4)\). A concentration of 0.03 organisms per g (i.e., \(-1.5\) log) in a sample is the concentration at which it is equally likely for the \([1/1, 0/3, 0/3, 0/3]\) and \([0/1]\) patterns to occur in the MPN enumeration, according to calculations by a previously reported method \((10)\) and data not shown. When the concentration for a product is \(<0.03\) organisms per g, the chance that a 25-g sample is negative is \(>50\%\) (i.e., there is a \(<50\%\) chance that the sample would be positive with an MPN pattern of \([1/1, 0/3, 0/3, 0/3]\) and \([0/1]\) patterns to occur in the MPN enumeration, according to calculations by a previously reported method \((10)\) and data not shown. The concentration distribution, once identified for use in the risk assessment, was divided into approximately 65 intervals by inputting the function into Analytica and running simulations (30,000 iterations). The \(-65\) intervals were obtained as follows: first, the concentration distribution was divided into 60 intervals with equal probability steps (i.e., equal increments on the \(y\) axis of the cumulative distribution function plot) in a simulation run; second, several additional intervals were identified in additional runs to obtain more intervals within 1-log ranges for levels of \(>1\) log CFU/g. In the analysis, we found that doubling the intervals in the first step (i.e., to 120 intervals) had little impact on the outcome of the analysis, while the additional intervals obtained in the second step allowed a more accurate calculation of the number of cases attributable to servings with contamination levels cumulative to \(\geq 1\) log CFU/g.

To reflect the highest concentration observed in the food survey, where necessary, a distribution with an infinite range, such as a gamma distribution, was truncated at an upper limit of 7.00 log CFU/g during the simulations. The interval data were used in the discreet stepwise process to derive the exponential model parameter \(R\) according to the approach described by Buchanan et al. \((5)\).

RESULTS AND DISCUSSION

Prevalence and distribution of concentrations in foods. \(L.\) monocytogenes contamination in the RTE foods investigated was determined on the basis of two variables: prevalence and concentration. Of 31,705 samples examined, 577 tested positive \((16)\), for an overall prevalence rate of 1.82\%. The 2.5th and 97.5th percentiles of the \(L.\) monocytogenes prevalence uncertainty distributions for the products were 1.68 and 1.97\%, respectively. The lower and upper bounds, as well as the observed prevalence, were used in the risk assessment. The concentration of \(L.\) monocytogenes in the positive samples varied by more than six orders of magnitude, from as low as \(-2\) to \(-1\) log CFU/g to as high as 5 to 6 log CFU/g. The frequencies of concentrations in various ranges are shown in Figure 1A. The relative frequency for each range was determined as the ratio of the number of samples with concentrations in that range to 577 (the total number of positive samples).

We fit the frequency data to various probability distribution functions, including lognormal, normal, Weibull, gamma, and beta distributions. Three criteria were used to evaluate goodness of fit for a distribution. Among the various probability distribution functions we evaluated for fitting the categorized data, the beta \((0.29, 2.68, -1.69, 6.1)\) and gamma \((0.33, 2.96)\) \(-1.70\) models ranked first and second as the best-fit distributions according to the criterion for goodness of fit in BestFit, with root-mean-square errors of 4.6 \(\times 10^{-5}\) and 6.5 \(\times 10^{-5}\), respectively. There were four parameters for the beta distribution, with the third and fourth parameters denoting the lower and the upper boundaries. The beta model exhibited a better visual fit to the data than the did the gamma model when the data were plotted in a cumulative curve (Fig. 1B). Figure 1C (a density curve) appears to show that the area of poorer fit for both models is in the range of \(-2\) to \(-1\) log CFU/g. In fact, the beta model predicts 394 positive samples in that interval, and 402 positive results were observed; the gamma model predicts 379 positive samples. Moreover, the density curve in this case is misleading in that one is unable to see the differences at the high concentration levels (the area of interest in this risk assessment) in it; these differences can be seen in the cumulative curve (Fig. 1B). The third criterion we used to determine whether a model actually did fit was as follows. A probability distribution that fits the data well will provide a 95th-percentile concentration between 1 and 2 log CFU/g, consistent with the observed data. The 95th percentile of the empirical distribution function (i.e., the data) occurs in the interval 1 to 2 log CFU/g, which has an observed frequency of 20/577 (Fig. 1A). With the use of this frequency and on the basis of a theory described previously \((24)\), a standard error of the empirical estimate of the 95th percentile would be \(\sqrt{0.05 \times 0.95 \times 577/20} = 0.26\). The beta model gave a 95th-percentile value of \(1.67\) log CFU/g, which satisfied this criterion. The gamma model gave a 95th-percentile value of \(2.58\) log CFU/g, an overestimate of the observed frequency data, which would result in a lower value of the dose-response model parameter \((R)\) than that based on the beta model (see Fig. 2).

In the simulations used to generate the concentration interval data for the dose-response analysis, the maximum concentration resulting from the beta distribution was 6.03 log CFU/g, which was in good agreement with the ob-
FIGURE 1. Distribution of *L. monocytogenes* concentrations in samples of ready-to-eat foods in which the organism was detected. (A) Numbers above bars are the numbers of samples in each concentration range (totaling 577 positive samples). (B) Open circles represent observed cumulative frequencies at or below the concentration indicated. (C) Open circles represent observed frequencies in each of the 1-log concentration ranges. In panels B and C, solid and dashed lines represent the probability distribution functions beta (0.29, 2.68, −1.69, 6.1) and gamma (0.33, 2.96) −1.70, respectively.

FIGURE 2. Exponential dose-response models derived from concurrent food survey and illness data collected at Maryland and northern California FoodNet sites. (A) The models defined by the respective $R$ values: $1.76 \times 10^{-10}$ (solid curve, based on the beta concentration model) and $7.80 \times 10^{-12}$ (dashed curve, based on the gamma concentration model). (B) Extrapolation of the dose-response models to low concentration levels by the plotting of log probability versus log CFU. Solid and dashed lines represent the models with $R$ values of $1.76 \times 10^{-10}$ and $7.80 \times 10^{-12}$, respectively.

Dose-response analysis. With the use of the dose-response analysis approach described by Buchanan et al. (5), a median prevalence of 1.82%, and the concentration distribution represented by the beta model, our data produced an $R$ value of $1.76 \times 10^{-10}$. If we used the gamma model instead to represent the concentration distribution for *L. monocytogenes* in the foods, we obtained an $R$ value of $7.80 \times 10^{-12}$. The dose-response curves are shown in Figure 2. Although the beta distribution provided the best fit, analysis observed maximum level ($5.18 \log \text{CFU/g}$ (16)). The maximum concentration resulting from the gamma distribution was, in truncation, 7.00 log CFU/g. We chose the beta model to represent the distribution of *L. monocytogenes* concentrations in contaminated RTE foods in the subsequent analyses. The 95th-percentile concentration level represented by the beta distribution (1.67 log CFU/g) was used for the analysis undertaken to derive an exponential dose-response model.
was carried out with both models merely to illustrate the impact that the distribution of concentrations (i.e., uncertainty of distribution) has on the dose-response model.

In two previous studies involving data specific to Germany (5) and Sweden (27), R values of $1.18 \times 10^{-10}$ and $5.6 \times 10^{-10}$, respectively, were estimated, suggesting that food servings contaminated with L. monocytogenes at low levels contribute to a minuscule risk of listeriosis. Both of these studies were based on the assumption that all listeriosis in the country under study resulted from the consumption of food from a single category, i.e., smoked or smoked-gravad fish. Since L. monocytogenes has been reported to occur in a wide variety of RTE foods in the United States (22, 26, 39), we assessed exposure on the basis of data from a survey of eight categories of RTE food products that are common in the American diet and should represent to a greater extent the baseline levels of L. monocytogenes exposure for U.S. consumers in the regions comprising the FoodNet sites (16).

A lack of geographical and temporal correspondence between food survey and illness data and uncertainty with regard to the accuracy of the illness data are potential weaknesses of the previous studies (5, 27). Besides the large sample size, unparalleled by any study previously conducted to quantify the occurrence of L. monocytogenes in RTE foods, the collection of the exposure data used in our study was concurrent with that of illness data from FoodNet surveillance in the same geographical locations (16). The CDC conduct active surveillance of listeriosis cases at the FoodNet sites, providing an estimate of illness data that is as accurate as is currently possible.

The results of our study, which addressed the potential weaknesses in the previous studies (5, 27), are strikingly similar to the results of those studies in that the likelihood of contracting listeriosis from the consumption of a single cell of L. monocytogenes is found to be extremely small. Our results indicate that the probability that illness will result from the ingestion of a single cell (approximately equal to the R value) is less than one in one billion ($1.76 \times 10^{-10}$) for people at increased risk on the basis of contamination levels represented by the beta probability distribution (Fig. 2). The y intercept in Figure 2B represents the logarithm of the probability that listeriosis will result from the consumption of one organism ($\log \text{CFU} = 0$), i.e., $\log_{10}$ of the R value. The likelihood of one’s acquiring listeriosis from the consumption of any given number of cells is readily determined from the model (Fig. 2B). For example, the consumption of $10^2$ CFU would result in listeriosis with a likelihood of $-7.8 \log$ (on the basis of the model with the solid line), which is equivalent to once in $10^{7.8}$ times a dose of $10^2$ CFU is consumed.

This R value estimate is conservative in that we assumed that the levels of the organism did not increase between purchase and consumption. Inclusion of the potential growth of the organism after the purchase of the product, during refrigerated storage in a consumer’s home, would increase the frequency of exposure at higher concentration levels and shift the concentration distribution to the right. This outcome is analogous to a shift from the beta curve to the gamma curve (Fig. 1B), which results in an increase in the concentration corresponding to the 95th percentile of concentrations. This implies that for the maintenance of consistency with the number of reported illnesses, the value of R must be decreased, which would result in a corresponding shift of the dose-response curve to the right, from the solid curve in the direction of the dashed curve (Fig. 2). In other words, the same number of illnesses would be accounted for by the consumption of a larger number of organisms, thus driving down the risk of illness per organism. The underestimation of the concentrations of L. monocytogenes to which consumers were exposed results in a higher, or more conservative, estimate of risk per organism in our risk assessment.

The exponential dose-response model gives a direct indication of the probability of illness as a result of the consumption of a given number of organisms. We have shown that regardless of the food category, consumers are exposed to a distribution of L. monocytogenes levels in RTE foods (Fig. 1) (16). Next, we addressed the question of which levels of contamination (CFU/g) in the food servings eaten by consumers contribute the most to illnesses. The answer to this question would provide a basis for the development of sound risk management strategies to control the pathogen in food and, ultimately, to reduce the risk of listeriosis to consumers.

Risk management strategies. The risk posed by L. monocytogenes in food to a highly susceptible individual is influenced by many factors. We reported on the prevalence and concentration of the organism in foods (16). We know the estimated numbers of listeriosis cases from CDC FoodNet surveillance. In addition to these factors, there are other variable factors that influence the likelihood of one’s contracting listeriosis from food servings contaminated at a given concentration level. We focused on the levels of L. monocytogenes in foods and made simplifying assumptions about the other factors: number of servings consumed, serving size, and size of the population at higher risk. We obtained estimates for these factors and used them, with their values remaining unchanged, as relative components in the risk assessment.

Under the conservative assumption that all L. monocytogenes exposure came from the eight food categories and on the basis of the exponential model whereby the probability of illness increases as the number of cells consumed increases, we found that the majority of the listeriosis cases were due to the consumption of those servings contaminated at higher concentrations (Table 1). On the basis of an estimate of 106 cases over the 2-year sampling period, only 0.22 cases would be attributed to the consumption of servings contaminated at concentrations of $\leq 10^2$ CFU/g (2 log CFU/g). On the basis of this model, 0.207% (median) of the incidence of listeriosis would be attributed to food servings contaminated at concentrations of $\leq 10^2$ CFU/g (2 log CFU/g). On the basis of this model, 0.207% (median) of the incidence of listeriosis would be attributed to such levels of exposure (Table 2). The pattern shown in Table 1, in which cases of illness are allocated across the entire spectrum of contamination levels, holds true after taking into account the uncertainty associated with our estimates of L. monocytogenes prevalence. On the
basis of the beta model for concentration distribution, the lower bound and upper bound prevalences would predict that 0.191 and 0.225% of the cases, respectively, would result from the consumption of servings contaminated at concentrations of $10^2$ CFU/g.

Preliminary data from the CDC (1) indicate that the frequency of listeriosis cases in the regions comprising the FoodNet sites and during the 2 years of our food survey (16) was consistent with a national estimate of 1,700 to 2,500 cases per annum. With the use of the dose-response analysis approach, an estimate of 1,700 cases per annum, a national consumption estimate of $1.11 \times 10^{10}$ servings for the eight product categories, and the beta concentration model to represent $L. monocytogenes$ concentrations, we obtained an $R$ value of $1.34 \times 10^{-10}$. If we used an estimate of 2,500 cases per annum instead, we obtained an $R$ value of $1.97 \times 10^{-10}$. On a national scale, the relative contribution to illness by food servings contaminated at concentrations of $\leq 10^2$ CFU/g was similar to that obtained for the two FoodNet sites (i.e., 0.19 to 0.22% of the cases occurring each year in the United States would be attributed to such levels of exposure [data not shown]).

It is clear that the most effective efforts to reduce the risk of listeriosis in RTE foods will involve targeting the food servings that are heavily contaminated, even though the fraction of those servings is very small. For example, on the basis of a 1.82% overall prevalence, 0.091% of the servings (1.82% $\times (1 - 0.95)$) would be contaminated at a concentration above the 95th-percentile level (estimated to be $1.67 \pm 0.26$ log CFU/g), and an even more minute fraction would be contaminated at higher concentrations (Fig. 1B).

Taking the analysis one step further, we assessed the level of risk reduction that would result from the application of various risk management approaches. The zero tolerance strategy is in essence a prevalence-oriented approach that does not distinguish foods contaminated at high concentrations from those contaminated at low concentrations. With the concentration distribution unchanged, a 50% reduction in prevalence would result in a 50% risk reduction, e.g., from 106 to 53 cases (Table 3). Alternatively, with the prevalence unchanged, a control strategy that stipulates a maximum $L. monocytogenes$ concentration of $10^8$ CFU/g for all servings would reduce risk by 89%, e.g., from 106 to 12 cases, on the basis of the beta concentration distribution and the associated exponential model parameter. The targeting of a maximum concentration at a lower level would achieve an even higher level of risk reduction than a 50% reduction in prevalence would. A control strategy that stipulates a maximum $L. monocytogenes$ concentration of $10^2$ CFU/g for all servings would result in a 99.5% risk reduction, e.g., from 106 cases to <1 case (Table 3).

Clearly, a risk management approach that actively manages the levels of $L. monocytogenes$ can have a greater impact on the reduction of cases of listeriosis than sole reliance on the reduction of the organism’s prevalence (i.e., zero tolerance).

### Table 1. Contributions of RTE food servings contaminated at or below various levels to listeriosis cases at two FoodNet sites

<table>
<thead>
<tr>
<th>$L. monocytogenes$ level (log CFU/g) in servings</th>
<th>Contribution of servings to listeriosis (cases/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.0063</td>
</tr>
<tr>
<td>1.0</td>
<td>0.034</td>
</tr>
<tr>
<td>2.0</td>
<td>0.22</td>
</tr>
<tr>
<td>3.0</td>
<td>1.3</td>
</tr>
<tr>
<td>4.0</td>
<td>7.5</td>
</tr>
<tr>
<td>5.0</td>
<td>29</td>
</tr>
<tr>
<td>6.03 (maximum)</td>
<td>106</td>
</tr>
</tbody>
</table>

$a$ A total of 53 cases were reported in Maryland and northern California in 2000 and 2001. The number was doubled to 106 to account for potential underreporting as per Mead et al. (28).

$b$ Cumulative number of cases for servings contaminated at or below the indicated level, based on a median 1.82% prevalence, the baseline concentration distribution, and the exponential dose-response curve with an $R$ value of $1.76 \times 10^{-10}$.

### Table 2. Influence of prevalence uncertainty on estimated listeriosis cases resulting from the consumption of RTE food servings contaminated with $L. monocytogenes$ at or below $10^2$ CFU/g at two FoodNet sites

<table>
<thead>
<tr>
<th>Prevalence (%)</th>
<th>Number (%) of cases ($n = 106$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.68 (lower bound)</td>
<td>0.202 (0.191)</td>
</tr>
<tr>
<td>1.82 (median)</td>
<td>0.219 (0.207)</td>
</tr>
<tr>
<td>1.97 (upper bound)</td>
<td>0.238 (0.225)</td>
</tr>
</tbody>
</table>

### Table 3. Predicted numbers of cases for all servings under various scenarios

<table>
<thead>
<tr>
<th>$L. monocytogenes$ concn$^a$</th>
<th>Baseline$^b$</th>
<th>Decreased by 50%</th>
<th>Increased by 100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (beta distribution)</td>
<td>106</td>
<td>53</td>
<td>212</td>
</tr>
<tr>
<td>Decreased to a maximum of $10^6$ CFU/g</td>
<td>11.9</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Decreased to a maximum of $10^2$ CFU/g</td>
<td>0.55</td>
<td>—</td>
<td>1.10</td>
</tr>
</tbody>
</table>

$^a$ Concentrations are levels given by the baseline distribution or by the same distribution truncated at the set maximum level, e.g., $10^2$ CFU/g.

$^b$ Prevalence baseline is the observed frequency, which is allocated across the concentration spectrum of the beta distribution (shown in Fig. 1B). When a maximum concentration is set, the fraction representing servings contaminated at a higher level is added to the fraction at the set level, e.g., $10^2$ CFU/g.

A total of 53 cases were reported at two U.S. FoodNet sites (Maryland and northern California) in 2000 and 2001. The number was doubled to 106 to account for potential underreporting as per Mead et al. (28). —, not calculated.

Overall prevalence rate, 1.82%.
erance for all RTE foods). This approach is especially effective when RTE foods that support *L. monocytogenes* growth are differentiated from those that do not, i.e., those for which populations of the organism will remain constant or diminish during shelf life.

It might be argued that the reorientation of risk management strategies to focus on concentration could result in less diligence in controlling the presence of *L. monocytogenes* and, consequently, in an increased prevalence of the pathogen in the food supply. Increases in prevalence would result in proportional increases in the predicted numbers of cases, e.g., from 106 to 212 cases, if concentration were not addressed. However, even with a twofold increase in prevalence, the level of risk reduction that would be achieved with a concentration-oriented control strategy stipulating a maximum concentration of $10^2$ CFU/g would still be about 99% (e.g., from 106 to 1.10 cases). This outcome contrasts with the scenario in which prevalence alone is reduced by 50%, resulting in a decrease from 106 to 53 cases (Table 3).

**CONCLUSIONS**

The level of risk that is “acceptable” is ultimately decided by society. Although the ideal level, i.e., zero prevalence and zero cases from the consumption of foods, cannot be reached, control measures would be most effective in reaching a goal of the lowest achievable incidence of illness if they were directed toward those products that currently contribute the most to the listeriosis cases in the FoodNet sites examined and, by extrapolation, in the United States. It is important to recognize that because of the ubiquitous nature of the organism, *L. monocytogenes* is present in RTE foods being consumed by U.S. consumers regardless of the zero tolerance policy. Our study provides an assessment of the predicted outcomes of various risk management strategies based on our current state of knowledge about the influential factors.

A maximum concentration of $10^2$ CFU/g at the point of consumption for foods that do support the growth of *L. monocytogenes* is part of a Canadian regulatory policy. This criterion is also accepted in several European countries (17). In spite of policies differing from the U.S. policy, the incidence of listeriosis reported in these industrialized countries is not noticeably different from the incidence in the United States (23). The estimated incidence is 3 to 4 cases per million people in Germany, Sweden, and Canada (21, 23). As our results clearly indicate, foods containing low levels of *L. monocytogenes* (e.g., $<10^3$/g) pose very little risk; eliminating the higher concentrations can reduce the number of predicted cases by >99%. No comparable reduction can be anticipated with the current emphasis on prevalence alone on the basis of recent FoodNet data (8).

Since limited resources are available to regulatory agencies and the industry, it would be more effective to direct these resources at foods in which *L. monocytogenes* is likely to be present and is likely to grow to high levels rather than targeting all RTE foods. This type of risk management strategy should not result in a negative impact on public health, as indicated by rates of listeriosis in countries that use such a strategy.

Developments within the last decade have led to a better understanding of the types of foods that support the growth of *L. monocytogenes*. A non–zero tolerance policy would encourage the development of measures to minimize the growth of the organism in foods by, for example, the application of multiple-hurdle technologies (25, 31) in product formulation and storage. In addition, such a policy would encourage the targeting of resources to develop more effective measures to reduce *L. monocytogenes* levels in finished products. These efforts would not compromise the safety of the food supply but, rather, would help to achieve the national goal of a reduction of illnesses caused by the consumption of *L. monocytogenes* in foods.

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